REMARKS

In view of the above amendments and the following remarks, reconsideration and further examination are respectfully requested.

Claim Amendments

Claim 3 has been canceled without prejudice. Claims 1, 5, 7, 8, 12, and 20 have been amended, and claims 21-31 have been added. It is believed that new claims as well as the amended claims are supported by the application as originally filed. For example, support for claim 1 can be found at paragraphs [0029] (p. 8) and [0056] (p. 12) as well as elsewhere throughout the application. Support for claims 21-24 can be found at claims 5, 8, and 20 as originally filed as well as elsewhere throughout the application. As another example, support for claims 25-31 can be found in paragraphs [0024]-[0029] (pp. 7-8) and [0049]-[0061] (pp. 10-13) as well as elsewhere throughout the application. As a result of these amendments, claims 1-2, and 4-31 are currently pending and under consideration.

Claim Objections

In item 3 of the Office Action, claims 1, 3, and 7 were objected to because of informalities. Claims 1and 7 have been amended to correct the cited informalities, and claim 3 has been canceled for incorporation into claim 1 (as discussed below).

Claim Rejections Under 35 USC §112

Claims 5, 8, and 20

In item 5 of the Office Action, claim 5, 8, and 20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Specifically, it was asserted that "A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired." As can be seen, the above-mentioned these claims have been amended and new claims 21-24 have been added to correct the cited informalities.

Claim 6

In item 6 of the Office Action, claim 6 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Specifically, it was asserted that "The wording of Claim 12 makes it unclear as to what is being claimed." Claim 12 has been amended in a manner, which is believed to help clarify claim 12.

Claim Rejections Under 35 USC §101

Claims 1-20

In item 8 of the Office Action, claims 1-20 were rejected under 35 USC 101 "because the claimed invention is directed to non-statutory subject matter." Independent claim 1 has been generally amended in the manner as was suggested in the Office Action to correct the cited informality.

Claim Rejections Under 35 USC §102/103

Independent Claim 1

In item 10 of the Office Action, independent claim 1 was "rejected under 35 U.S.C. 102(b) as being anticipated by Ward et al. (International Application WO 02/07585 A2)." Independent claim 1 has been amended to incorporate the features of dependent claim 3 as well as to highlight some of the unique features of the present invention. It is believed that claim 1, as currently amended, is allowable over the references of record. For example, Ward fails to disclose or suggest "an inbound light guide in which primary light is conducted through the skin surface into the interior of the body, the primary light having a wavelength of at least 550 nm and at most 900 nm" and "wherein the light irradiation surface of the inbound light guide and the light receiving surface of the detection light guide are adapted to be located subcutaneously so that the test volume contains interstitial fluid" as is now recited in claim 1.

The inventors for the present application developed a unique and inventive reagent free analysis system for determining the concentration of analyte, which is well suited for continuous monitoring. Specifically, the inventors discovered that it was possible to determine the concentration of analytes, such as glucose, subcutaneously using light having a wavelength between 550 and 900 nm with Raman analysis. As discussed throughout the present application, background fluorescence is a major source of interference that inhibits Raman analysis. The

inventors discovered a significant improvement in the signal to noise ratio (S/N) when the above-mentioned wavelength range was used for Raman analysis. As discussed in paragraphs [0029] (p. 8) and [0056] (p. 12) as well as elsewhere throughout the application, the inventors found that the intensity of Raman-scattered light significantly increased; while at the same time, the interfering fluorescence significantly reduced in this range. It was further found that interstitial fluid is particularly suited Raman spectroscopy because interstitial fluid contains far fewer fluorescence molecules than blood (paragraph [0026], pp. 7-8).

In contrast, Ward does not disclose the above-mentioned wavelength range for Raman analysis, and only in passing does Ward mention analyzing interstitial fluid at all. Ward mainly discusses the concept of detecting shock in patients during emergency medical situations. In such situations, blood samples are typically readily available, and in fact, all of the figures in Ward refer either to blood or to extracorporeal examination of muscles in animals, and not to subcutaneous analysis. For Raman analysis, Ward on page 15 merely teaches that "resonance Raman spectroscopy according to the invention is performed at a deep ultraviolet wavelength, i.e., at 390 to 420 nm" which is clearly outside the range recited in claim 1. When Ward does mention other wavelength ranges, it is with respect to other analysis techniques, like absorption spectroscopy or fluorescence. In the only real discussion of interstitial fluid, Ward on page 37 teaches the use of wavelengths that are even farther away from the above-recited range by stating "Resonance Raman spectroscopy in the deep ultraviolet wavelength (less than 270 nm) is used for interstitial fluid analysis." Considering that Ward fails to disclose either expressly or inherently all of the features recited in claim 1, claim 1 is not anticipated by Ward.

In addition, the features recited in claim 1 would not have been obvious to one of ordinary skill in the art. As discussed in the present application, there are a number of significant difficulties associated Raman analysis would have lead one skilled in the art away from the combination of features recited in claim 1. Ward does not even recognize or address these issues, such as difficulties associated with fluorescence interference. The analytes discussed at length in Ward, oxy/deoxy hemoglobin and NDA/NADH (or NADPH), provide strong Raman signals, and thus, Ward would not need to address interference issues. It should also be noted that in Raman spectroscopy the intensity of the signal drops by the 4^{th} power of the wavelength (see also, paragraph [0028], p. 8). In other words, one skilled in the art would have expected that doubling the wavelength would reduce the intensity of the Raman signal to $1/16^{th}$ of the original

value. Thus, one skilled would not have expected successful Raman analysis at the relatively long wavelengths required for analytes, such as glucose, and thus, one skilled in the art would not have been motivated to arrive at the combination of features recited in claim 1. For these and other reasons, it is submitted that claim 1 and its dependent claims are allowable over the references of record.

In addition to the reasons given above for the allowability of independent claim 1, other reasons support the patentability of its dependent claims. In item 13, dependent claim 7 was "rejected under 35 U.S.C. 103(a) as being unpatentable over Ward et al. as applied to Claim 1 above, and further in view of Haar et al. (PCT Application WO 99/07277) which corresponds to Haar et al. (US Patent 6,584,335)." In particular, it was alleged that it would have been obvious "to have provided the analyte concentration determining device of Ward et al. with a semipermeable membrane covering the fiber optic probe as taught by Haar et al. in order to avoid the interfering effects associated with large molecules in the interstitial liquid." Granted, the use semipermeable has been described before in Haar. However, there is no disclosure that this feature would be particularly helpful or useful in the context of Raman spectroscopy, especially in the claimed wavelength range. As discussed in paragraph [0056] (p. 12) of the present application, there is a significant reduction fluorescence interference when such a semipermeable is used in conjunction with the recited wavelength range. Except for impermissible hindsight, there would have been no proper motivation to use such a semipermeable membrane in conjunction with Raman analysis at the wavelength range recited in claims 1 and 7. For these and other reasons, claim 7 is allowable over the references of record.

Independent Claim 25

It is believed that new independent claim 25 is allowable over the references of record. For example, Ward as well as the other references of record fail to disclose or suggest "shining a monochromatic primary light that has wavelength of at least 550 nm and at most 900 nm from the light irradiation surface of the sensor head into the test volume containing the interstitial fluid." As noted before, Ward fails to disclose or suggest this recited wavelength range, especially with respect to Raman analysis. Moreover, except through impermissible hindsight there would have been no motivation to arrive at this feature as well. In addition, Ward fails to expressly or inherently teach "wherein said inserting includes locating the light irradiation surface and the light receiving surface in subcutaneous connective tissue of the skin so that a test volume of the sensor head contains interstitial fluid" as is recited in claim 25. For these and other reasons, independent claim 25 and its dependent claims are allowable over the references of record.

Power of Attorney

As a housekeeping matter, it should be noted that a Power of Attorney to Prosecute Applications Before the USPTO for Roche Diagnostics Operations, Inc., and a Statement Under 37 CFR 3.73(b) for this application have been enclosed with this response in order to update the Power of Attorney to the current customer number (41577). It is believed that the requirements to update the Power of Attorney for this application have been satisfied, but if additional documentation is required, the Examiner is invited to contact the undersigned by telephone to quickly resolve the issue.

Conclusion

It should be understood that the above remarks are not intended to provide an exhaustive basis for patentability or concede the basis for the rejections in the Office Action, but are simply provided to overcome the rejections made in the Office Action in the most expedient fashion.

In view of the above amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and an early notice of allowance is earnestly solicited. If after reviewing this amendment the Examiner feels that any issues remain which must be resolved before the application can be passed to issue, the Examiner is invited to contact the undersigned representative by telephone to resolve such issues.

Respectfully submitted,

By /Charles P. Schmal #45,082/

Charles P. Schmal, Reg. No. 45082
Woodard, Emhardt, Moriarty, McNett & Henry LLP
111 Monument Circle, Suite 3700
Indianapolis, Indiana 46204-5137
(317) 634-3456